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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/831,954 | 06/25/2001 | Hubert Jan Jozef Loozen | O/98414-US | 9900 |

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| EXAMINER | |
|---|---|
| JIANG, SHAOJIA A | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1617 | 9 |

DATE MAILED: 04/09/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. 09/831,954 | Applicant(s) LOOZEN ET AL. | |
|---|---|---|---|
| | Examiner Shaojia A. Jiang | Art Unit 1617 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *23 January 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-5 and 7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

This Office Action is a response to Applicant's amendment and response filed on January 23, 2002 in Paper No. 7 wherein claim 6 is cancelled and claim 7 is newly submitted. Currently, claims 1-5 and 7 are pending in this application.

Applicant's amendment filed on January 23, 2002 in Paper No. 7 with respect to the rejection of claim 6 made under 35 U.S.C. 112 second paragraph and under 35 U.S.C. 101 for the claimed recitation of a use of record stated in the Office Action dated October 23, 2001 have been fully considered and found persuasive to remove the rejection since claim 6 is cancelled.

Applicant's remarks filed on January 23, 2002 in Paper No. 7 with respect to the rejection of claims 1-6 made under 35 U.S.C. 102(b) as being anticipated by Lobaccaro et al. for reasons of record stated in the Office Action dated October 23, 2001 have been considered and are found persuasive to remove this particular rejection.

Applicant's remarks filed on January 23, 2002 in Paper No. 7 with respect to the rejection of claims 1-2 and 5-6 made under 35 U.S.C. 102(b) as being anticipated by Napolitano et al. for reasons of record stated in the Office Action dated October 23, 2001 have been considered and are found persuasive to remove this particular rejection.

Applicant's remarks filed on January 23, 2002 in Paper No. 7 with respect to the rejection of claims 1-4 made under 35 U.S.C. 102(b) as being anticipated by Baran et al. (3,755,301) for reasons of record stated in the Office Action dated October 23, 2001 have been considered and are found persuasive to remove this particular rejection.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lobaccaro et al. (of record in the previous Office Action).

Lobaccaro et al. teach the active compounds, 11β-n-alkyl estradiol having ethyl, butyl, or decyl as $R_{11}$, which are homologs of the instant compounds, and their compositions. Lobaccaro also teaches that compounds therein are known estrogenic compounds. See abstract, Scheme 1 compound 5b on page 2218, Table 1 on page 2219, Table 2 on page 2221, and the 4$^{th}$ paragraph of page 2224.

Lobaccaro does not expressly disclose the particular 11β-n-alkyl estradiol herein having a length of from 5-9 carbon atoms, and the employment of these estradiol in a pharmaceutical composition and method for treating estrogen deficiency disorders.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ the particular 11β-n-alkyl estradiol herein in a pharmaceutical composition and method for treating estrogen deficiency disorders.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ the particular 11β-n-alkyl estradiol herein in a pharmaceutical composition and method for treating estrogen deficiency disorders since the estradiols of Lobaccaro are known estrogenic compounds and estradiol compounds are well known to be useful in pharmaceutical compositions and the method for treating estrogen deficiency disorders.

Moreover, the structure of the instant compounds having a length of from 5-9 carbon atoms in $R_{11}$, is substantially similar to the structures of their homologs having ethyl, butyl, or decyl as $R_{11}$ in Lobaccaro. Therefore, one of ordinary skill in the art would have reasonably expected that the instant compounds would have possess the similar activity as their homologs because of the substantially close structural relationship. It has been settled that the addition of $CH_3$ or several $CH_2$ groups to a known compound is not ordinarily patentable and prima facie obvious. See *In re Wood*, 199 USPQ 137. Thus, one of ordinary skill in the art would have reasonably expected that the instant compounds would be useful in the method for treating estrogen deficiency disorders, absent evidence to the contrary.

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Claims 1-5 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Napolitano et al. (of record in the previous Office Action).

Napolitano et al. teach the active compounds, 11β-substituted estradiol derivatives having $R_{11}$ with less than 5 carbon atoms, which are homologs of the instant compounds, and their compositions. Napolitano et al. teaches that 11β-substituted estradiol derivatives therein are known estrogenic compounds as the estrogen receptors. See abstract and Table 1 on page 2776.

Napolitano et al. does not expressly disclose the particular 11β-substituted estradiol herein having a length of from 5-9 carbon atoms, and the employment of these estradiol in a pharmaceutical composition and method for treating estrogen deficiency disorders.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ the particular 11β-substituted estradiol herein in a pharmaceutical composition and method for treating estrogen deficiency disorders.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ the particular 11β-substituted herein in a pharmaceutical composition and method for treating estrogen deficiency disorders since the estradiols of Napolitano are known estrogenic compounds and estradiol compounds are well known to be useful in pharmaceutical compositions and the method for treating estrogen deficiency disorders.

Moreover, the structure of the instant compounds having a length of from 5-9 carbon atoms in $R_{11}$, is substantially similar to the structures of their homologs having

about 5 carbons or less as $R_{11}$ in Napolitano. Therefore, one of ordinary skill in the art would have reasonably expected that the instant compounds would have possess the similar activity as their homologs because of the substantially close structural relationship. It has been settled that the addition of $CH_3$ or several $CH_2$ groups to a known compound is not ordinarily patentable and prima facie obvious. See *In re Wood*, 199 USPQ 137. Thus, one of ordinary skill in the art would have reasonably expected that the instant compounds would be useful in the method for treating estrogen deficiency disorders, absent evidence to the contrary.

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Applicant's results shown in the Example III of the specification at pages 12-16 herein have been fully considered with respect to the nonobviousness and/or unexpected results of the claimed invention over the prior art but are not deemed persuasive for the reasons below. Example III provides no clear and convincing evidence of nonobviousness or unexpected results over the cited prior art since there is no side-by-side comparison with the closest prior art. Therefore, the evidence presented in specification herein is not seen to support the nonobviousness of the instant claimed invention over the prior art.

For the above stated reasons, said claims are properly rejected under 35 U.S.C. 103(a). Therefore, said rejection is adhered to.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (703) 305-1008. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Minna Moezie, J.D., can be reached on (703) 308-4612. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-1235.

Shaojia A. Jiang, Ph.D.
Patent Examiner, AU 1617
April 1, 2002

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